THE UNIVERSITY OF CHICAGO

Round Table

ACTH and Cortisone: A New Era in Medicine

An NBC Radio Discussion by JOHN S. L. BROWNE
EDWARD C. KENDALL *and* ALLAN T. KENYON

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THE STORY OF COMPOUND E

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ACTH and Cortisone: A New Era in Medicine

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DR. KENYON: We plan to tell something of the story of an extraordinary event in medical research. ACTH and cortisone relieve the signs and symptoms of rheumatoid arthritis.[1] This was unforeseen. We have moved into a new world in research and in practice. Dr. Kendall, your own chemical work on the adrenal cortex at the Mayo Clinic has been in large part responsible for this new advance. What does it signify to you?

DR. KENDALL: Cortisone is a new tool with which it will be possible to study the cause and nature of many diseases which have long been known but for which there has been no satisfactory explanation or treatment.

DR. KENYON: Dr. Browne, you have contributed greatly to our understanding of adrenal cortical physiology. What does this new work mean to you?

DR. BROWNE: I feel that the discovery of Dr. Kendall and Dr. Hench is revolutionizing our concept of disease and has given us a new way of studying how the person can protect himself against them. It is indeed a new era in medicine.

DR. KENYON: The foundation for this new development was laid by many workers in many countries. Of necessity much important work must go unnamed today. Years of chemical, physiological, and clinical research taught us that the adrenal gland was a very important and interesting structure; that it was, indeed, essential to life. We came likewise to understand, as Dr. Browne will tell us, that various circumstances of stress, infections, excessive exercise, or exposure to cold, for example,

[1] ACTH is an abbreviation of adrenocorticotrophic hormone, a substance which is secreted by the pituitary gland located in man at the base of the brain. ACTH stimulates the adrenal gland, located above the kidneys, to secrete its compounds. One of these adrenal compounds, designated "Compound E" during its investigation, is now called cortisone.

made a sharp and urgent demand upon the adrenal gland and that th organism was vulnerable in several ways if this organ could not respond This was roughly the upshot of this line of work.

In the meantime, students of rheumatoid arthritis had examined thi disease. They had noted the variable and often chronic character of it course and had described in detail the inflammation in and about th joints which many times resulted in crippling deformity. The fever an several other elements in the illness suggested an infection, but no excit ing agent such as a germ or virus was ever surely identified as respon sible. Certainly no reason existed for supposing that the adrenal glan was defective in any way, and nothing accordingly suggested the use o adrenal materials in treatment. Today, matters are changed. The year of work on the adrenal cortex, on the one hand, and on this obscure dis abling disease, on the other, have reached a common focus. This surpris ing union was accomplished at the Mayo Clinic by Dr. Edward C Kendall, who had long been concerned with the chemistry of the adrenal cortex, and by Dr. Philip Hench, who had cared for thousands of pa tients with arthritis, seeking endlessly for some more effective way of helping them.

Dr. Kendall, will you tell us how this all came about? Then we will ask Dr. Browne about how this relates to the old problems of stress in animals and man and how the pituitary gland, the source of ACTH, comes into the picture. Then I will comment at the end.

DR. KENDALL: A chemical and physiological investigation of the adrenal cortex was begun in the laboratory of the Mayo Foundation nineteen years ago. The first step was to grind the glands. They then resembled soft hamburger. From this mass of fat, meat, and blood small amounts of pure white crystals were separated. The crystals were found to consist of a group of new compounds. They were designated A, B, C, D, E, and F. The chemical structure of these compounds was established, and four of them were found to have physiological activity. From one thousand pounds of adrenal glands of beef, the amount of Compound A which could be isolated was equivalent to one small white tablet. The supply of adrenal glands is limited to the number of cattle killed, and the amounts of A, B, E, and F which could be obtained in the laboratory was insignificantly small. For physiological investigation it was neces sary to confine our work to rats and mice and to a very few dogs. The

results were encouraging. But it was not possible to expand the use of these compounds to human beings, because the supply was so limited.

During these same years, Drs. Pfiffner and Wintersteiner, and Dr. Reichstein and his associates in Switzerland, also carried out similar chemical investigations. But there was no great interest in the manufacture of these compounds for human use until 1941. At that time there were rumors that the Germans were buying all the adrenal glands in the Argentine slaughterhouses, that these glands were extracted, and that the administration of the extract to the *Luftwaffe* pilots enabled them to fly at altitudes of forty thousand feet and fight without difficulty. The rumor persisted, even though untrue, and was a real stimulus to make Compounds A, B, E, and F more available. Conferences were called by the National Research Council in Washington. Many different methods for the manufacture of these compounds were explored. In 1944 a practical method to make Compound A was devised in my laboratory. In December, 1945, Merck and Company prepared a large sample by this method. In 1946 it was tried on animals and was found to be of value in protecting them against poisons and cold. But when Compound A was given to a patient whose adrenal gland had been destroyed by disease, it was found that it was valueless. This was a great disappointment and almost killed any further interest in the work.

Only one hope remained. That was to make and try Compound E, now known as cortisone. Compound E closely resembles Compound A, but it contains one more atom of oxygen. In 1946 Dr. L. H. Sarett of Merck and Company prepared a sample of Compound E, but the yield was very, very small. Nevertheless, Merck and Company decided to go ahead and make five grams of Compound E, or cortisone. To make cortisone requires many months of labor in the chemical laboratory. While this work was in process, many important improvements were discovered in my laboratory and in the research laboratory of Merck and Company. Indeed, new steps were introduced, with the result that not five grams, but several hundred grams—about a pound and a half—of cortisone was produced. I do not know the cost of this work, but it must have been several hundred thousand dollars.

Cortisone was ready for use in the summer of 1948. It was tried on a patient whose adrenal glands had been destroyed by disease and was found to be highly active. This was in striking contrast to the result with Compound A. However, the total amount required to treat all patients

who suffered from a deficiency of adrenal activity would be small. If this were the only use for cortisone, then it would have been a poor reward for all the effort that had been expended. I was a man with a new drug, but with little except hope for its future. Now it so happened that, at the Mayo Clinic, Dr. P. S. Hench had specialized in the study of rheumatoid arthritis for the last twenty-five years. During all this time he had been looking for a drug which would help. For the last ten or twelve years, we had had many conferences about the treatment of this disease. Dr. Hench had observed that patients with rheumatoid arthritis who became jaundiced were relieved of their pain. He also observed that if a woman with rheumatoid arthritis became pregnant, the symptoms of the disease were diminished or quite completely relieved. The chemical problem involved was to find what substance could produce both of these effects. A possible explanation for the clinical observations made by Dr. Hench was that, in both jaundice and pregnancy, the adrenal gland was stimulated to deliver an increased amount of its secretion.

Dr. Hench has a notebook which contains an entry made in January, 1941, "Try Compound E in rheumatoid arthritis." This note was made after one of our many conferences. Shortly after this time, however, Dr. Hench went into the medical corps of the Army and remained for four years. But in the summer of 1948 he was ready to try Compound E—that is, cortisone—on arthritis. He had asked me how things were going with the preparation of cortisone on many an occasion. I had always replied that it was not ready. Finally, in August, 1948, I could say, "Yes, it is ready." It was first used on a patient with rheumatoid arthritis on September 21, 1948. The results were encouraging. During the winter, with the cooperation of Drs. H. F. Polley and C. H. Slocumb, cortisone was used on fifteen more cases. On March 28, 1949, cortisone was first used on three cases of rheumatic fever. The results were equally encouraging. Since then, cortisone has been tried on patients with other diseases, and it is now apparent that cortisone has a wide application in the study and possible treatment of these diseases. After the publication of the results on patients, some confusion arose about the name "Compound E." The difference between Compound E and vitamin E was not clear. We gave Compound E the name "cortisone" to differentiate it from vitamin E.

Today, cortisone is in great demand. The supply is so limited that only about seventy cases can be treated. An important question is how and when the supply of cortisone can be increased. I wish that I could

make clear to you the great effort which is now being made in many different laboratories in this country and abroad.[2] Today, cortisone is made from the bile of beef. The supply of bile is limited. Other sources have been mentioned as possible starting material. One of these is the plant—*Strophanthus sarmentosus*—which has been found in Africa. Another is a plant which grows in Mexico. The African plant does not have seed until after five years of growth, and it is only the seed which furnishes the starting material to make cortisone. The Mexican plants would have to be cultivated; this would require many months or years. Apart from these, there is the hope that cortisone can be made from a constituent of soybean oil. But this has not yet been accomplished. Finally, there is the chance that the chemist can make cortisone from simple chemicals, not produced in either plants or animals, but found in

[2] On December 4, 1949, the *New York Times* reported the announcement of another method of producing cortisone. Revealed by a group of doctors from the Worcester Foundation in Shrewsbury, Massachusetts, the method consists of keeping the adrenal glands of slaughtered animals "alive" in a test tube. The isolated gland continues to live as it would in the animal body and produces valuable hormones which can be collected and used.

This does not mean that cortisone will be available in quantity at low cost now, but it is the first indication that large-scale production may be possible. Kept under conditions of life in a test tube, the adrenal glands of dead animals tirelessly perform the laborious and complicated steps required to synthesize cortisone in the laboratory.

To keep the gland functioning, it must be put under its laboratory conditions within a half-hour after the animal is slaughtered. In the laboratory, it is put into an arrangement of ordinary glass flasks and tubes, which is quite easily and inexpensively assembled. To keep the gland "alive," blood and oxygen are pumped into it through a device which simulates the rhythm and function of the human heart mechanically. The gland dies quickly unless natural infection is combatted by putting penicillin into the circulating fluid.

To produce cortisone, an inexpensive and readily available starting material, 11-desoxycorticosterone, is fed to the gland, which then produces between one and two grams of corticosterone per day. This substance is only one simple chemical step away from cortisone.

Although the starting materials and the equipment used in the process are inexpensive and readily available, the Worcester scientists cautioned that it would take time to transfer the process from the laboratory to industry and that there must be many further investigations before the adrenal hormones could be used, if ever, to treat many of the estimated seven million Americans afflicted with rheumatic diseases.

the laboratory. This would be a total synthesis of the compound. Cortisone is a complex molecule. Its total synthesis is one of the most difficult problems in the field of organic chemistry. But it cannot be excluded as a possibility; in fact, it is perhaps our best hope. It is also possible that something else will be found which can be made easily and which will be just as good as cortisone. Trial of several such compounds have yielded completely negative results.

I believe that the chance of finding an abundant substitute for cortisone is not good. Within recent years the work of many investigators has shown that nature has a way to make cortisone within the body. The pituitary gland elaborates a special agent which has been designated ACTH and which directly stimulates the adrenal gland. In this way the body makes its own cortisone. Dr. Hench and I asked Dr. John Mote of Armour and Company for some of this agent which had been prepared from the pituitary glands of hogs in the research laboratories of Armour and Company. On February 8, 1949, we gave this material to patients with rheumatoid arthritis and with rheumatic fever. The results showed that it was possible for the patient to make his own supply of cortisone through the stimulation furnished by the special agent ACTH.

DR. KENYON: Thank you very much, Dr. Kendall. Dr. Browne, I wonder if you could relate these extraordinary events to your own early experience with the adrenal acting under stress and tell us perhaps something more of how the pituitary body comes into the picture.

DR. BROWNE: In the last seventy-five years the attention of medicine has been directed to environmental damaging agents, such as germs and poisons which cause disease. It has been known, however, that the way in which the body responds to the damaging agent—the so-called "host response"—is of great importance in disease. The pneumococcus is not pneumonia, and different people react differently to it and to other damaging agents.

In 1936 Dr. Hans Selye of Montreal showed in experimental animals that the body reacts in the same way to a number of damages—burns, fractures, severe exercise. He showed that the adrenal cortex enlarges and increases its function in all these conditions. He called the sum total of the body's common response, including that of the adrenal, the "general adaptation syndrome." Guided by this view, over the last twelve years, our laboratory at McGill University Clinic, Royal Victoria Hos-

pital, Montreal, has studied various diseases in the human being. Dr. Venning and Dr. Weil showed that there is an increase in excretion of cortisone-like substances in the urine after burns and fractures, in pneumonia, in psychological stress, and in pregnancy. In addition to the adrenal response, protein metabolism and vitamin C metabolism also change in a similar way in a variety of diseases. Dr. Albright of Boston related the adrenal and the protein metabolism changes to each other. There thus seems to be a common response of the adrenal in a variety of diseases in the human being as well as in the animal. It is known that, if the adrenal is destroyed, the person cannot withstand pneumonia, a burn, or other severe injuries. The adrenal response thus protects the body against damage.

How does the increase in the adrenal function come about? Many years ago it was shown by many workers that the anterior pituitary gland at the base of the brain secretes a hormone which stimulates the adrenal cortex to enlarge and to secrete more of its hormones. This substance was called adrenocorticotrophic hormone, or ACTH. It was, over the years, extracted from pituitary glands and purified by Dr. J. B. Collip of the University of Western Ontario, Dr. Herbert Evans of California, and eventually by Doctors Li, Simpson, and Evans of California and Doctors Sayers, White, and Long of Yale. The Armour Company of Chicago then took up the preparation of ACTH from the pituitaries of hogs. With this available, Dr. George Thorn, Dr. Forsham, and their co-workers at Harvard, Drs. Hoffman, McAlpine, and McIntosh at McGill, and Dr. Conn of the University of Michigan studied the effect of ACTH in normal and diseased people. Following Dr. Kendall and Dr. Hench's discovery, as you have heard, ACTH was used in rheumatoid arthritis with good effect. Unfortunately, as in the case of cortisone, the supply of ACTH is very limited. From four hundred thousand hogs, only one pound can be made. The total amount of ACTH made in one year—that is, about sixty pounds—is enough to treat only three of every hundred thousand cases of rheumatoid arthritis. As in the case of cortisone, only if it can be made chemically can the amount of ACTH available be markedly increased.

In the past year, cortisone, supplied by Merck and Company through a national committee, and ACTH, supplied by the Armour Company through Dr. John R. Mote, have been tried by many workers in a wide variety of diseases other than rheumatoid arthritis. Definite and marked-

ly good effects have been observed. The great importance of this is that it makes possible research into the ways in which the body deals with disease. We can now affect the body's response at will. These new findings of the effects of cortisone and ACTH in many diseases confirm the view that the body protects itself in a similar way in many diseases which we medical men have up to now thought of as being separate and distinct and as having no connection with each other.

Unfortunately, because of the small supply, the number of people who can be treated is so small that cortisone and ACTH can be used only for research purposes. It should be remembered that in many diseases there are already methods of treatment which have been found satisfactory in the past and that this new discovery does not make these treatments less effective. Thus there are many agents other than cortisone and ACTH which are very effective in certain diseases—for example, penicillin and other antibiotics in infections, insulin in diabetes, and so forth. Many scientists all over the country are working on ways of making more cortisone and ACTH, of finding other substances or methods which may also assist the body in dealing with disease.

The discovery of Dr. Kendall and Dr. Hench is thus revolutionizing our concept of disease and has given us a new way, as I said before, of studying how the person can protect himself against them. It is indeed a new era in medicine.

Dr. Kenyon: Thank you, Dr. Browne. Thus an adrenal agent, long called Compound E by Dr. Kendall and now known as cortisone, and a pituitary agent, known as ACTH, both relieve the inflammatory process in rheumatoid arthritis, abolish the fever, and restore appetite and a sense of well-being. Cortisone acts directly on the tissues. ACTH acts upon the adrenal, causing this gland to secrete cortisone or some near-relative, which in turn acts upon the tissues. However dramatic the effects, and they are indeed so, we cannot consider now that either agent cures rheumatoid arthritis. On this point both Dr. Hench and Dr. Kendall and many others have been most explicit. If the disease is severe and progressive, the symptoms often return after the hormone is stopped. As Dr. Browne has so well emphasized, we must suppose that cortisone modifies the reaction of the patient—of the so-called "host"—rather than removes the fundamental exciting agent of the disease. It is not another penicillin, destroying a germ. That would be a cure. It is rather an

extraordinary influence that fortifies the tissues against the ravages of the still persisting and still mysterious agent of rheumatoid arthritis. When this beneficial protecting influence of the hormone is withdrawn, the disease accordingly returns.

Something of this same beneficial effect may be seen in other illnesses with cortisone or ACTH. Dr. Kendall has spoken of rheumatic fever. Here again there is no reason to suppose that the fundamental cause is removed. The alleviation of symptoms appears real enough, but how long does this relief last after the hormone is stopped if the exciting agent of the disease is not eliminated? This is one of the many questions concerning rheumatic fever which has not been fully answered. It will thus take some time before the actual benefits of ACTH and cortisone can be properly measured.

To return to rheumatoid arthritis, where long-continued treatment with high dosage of adrenal materials is often clearly necessary to maintain relief. Such treatment has its hazards which we must learn to avoid. Chronic overdosage of the body with adrenal hormones has long been known to produce the disorder known as Cushing's syndrome. Tumors of the adrenal cortex may produce this disease by secreting an excess of cortisone-like material. A ruddy discoloration of the skin, obesity of a peculiar type, high blood pressure, and diabetes mellitus are among the symptoms. It now appears that elements of this disorder may be produced by the high dosage of cortisone or ACTH used in the treatment of rheumatoid arthritis. These symptoms, which have been clearly described by the Mayo group, subside when treatment is stopped. Dr. Kendall feels confident that such unfortunate effects can be avoided by proper management, but it will be some time before a complete evaluation of this margin of safety in all circumstances is accomplished. These and other considerations too complex for discussion here illustrate the many problems of research that must be answered before the wise use of this new and powerful agent can be assured. In the meantime, patients should not neglect the ordinary means of treatment which have their own proved worth as well as their limitations.

I think that we should close on the note of high expectation which Dr. Kendall sounded when he spoke of cortisone as a new tool for the study of obscure disease. Dr. Browne has outlined the reaction of the adrenal to many kinds of stress, and Dr. Kendall has shown how appreciation of this reactivity of the adrenal led in time to the discovery of

the effects of cortisone and ACTH on rheumatoid arthritis. The full extent of the protective effects of the adrenal hormone on the tissues of the body, however, were not understood before this new discovery. Many influences of this hormone had been known, and the adrenal cortex had been considered vital in several particulars. But that a chronic and disabling inflammatory process like that of rheumatoid arthritis could actually represent an unsatisfied need for adrenal hormone? This was never predicted. It is now seen to be, however, the almost unbelievable truth. The need for adrenal materials has been before us all along in the shape of familiar illness. This, I think, is the heart of this revolution in our thinking about disease. The body lacking the full protective influence of adrenal hormones falls ill. This illness may express itself in chronic and disabling inflammatory disease. Need for adrenal hormone therefore takes an unexpected form—a form doubtless influenced by the nature of the exciting agent of the disease and by the peculiarities of the individual tissues. As the adrenal hormone repairs and controls many elements in these disorganized reactions of the patient, it becomes a tool for their study, a means for perfecting our knowledge of the response of the patient. The sulfa drugs and penicillin represent a great modern advance aimed at the exciting agents of disease. This new work on ACTH and cortisone described by Dr. Kendall and Dr. Browne is aimed in another direction—at the sick body itself that exciting agents injure—at the protection of the host, as Dr. Browne has emphasized.

THE STORY OF COMPOUND E*

*

IN APRIL, 1949, newspapers told a story vitally important to millions of the American people. "New Hormone Hailed by Arthritis Experts," "Relief for Arthritis in New Discovery," they screamed in headlines. The story originated at the Mayo Clinic in Rochester, Minnesota. Excellent results had been obtained by Dr. Philip S. Hench, a member of the medical and scientific committee of the Arthritis and Rheumatism Foundation, and his associates in treating rheumatoid arthritis patients with "Compound E," discovered by Dr. Edward C. Kendall, Mayo Clinic chemist.

Arthritis victims and their families sent countless inquiries about Compound E to the Mayo Clinic, to the Arthritis and Rheumatism Foundation, to Merck and Company, the manufacturing chemists who made the substance available in some quantity to Dr. Hench.

This article provides the answers to many questions asked about Compound E or "cortisone," as Dr. Kendall prefers to call it.

It Began in War Research

Cortisone (17-hydroxy-11-dehydro-cortico-sterone), a hormone secreted by the suprarenal (or adrenal) glands of cattle, was isolated in its natural state by Dr. Kendall in 1935. After the outbreak of World War II reports from Europe indicated that German aviators had been able to resist the effects of high altitude flying after receiving injections of suprarenal gland extract. Stimulated by these reports, the United States Office of Scientific Research and Development decided to see what could be done in this country with Dr. Kendall's discovery.

The first problem was the production of a sufficient quantity of the hormone to use in experimental tests. Accordingly, the research chemists of Merck and Company were invited to work with Dr. Kendall. In January, 1942, the project was under way.

World War II was won before some of the difficulties of production were finally overcome in 1946. Two more years passed before enough cortisone had been accumulated to permit testing. By that time the inter-

* Reprinted by special permission from *Hygeia,* September, 1949.

est of the Air Force and Navy had waned, and the substance was made available to Dr. Hench for trial on patients with rheumatoid arthritis.

The value of cortisone in aviation medicine or for the treatment of shock and fatigue is still speculative.

Jaundice and Pregnancy Gave Clues

Dr. Hench's request for cortisone was not a shot in the dark.

For many years the most promising "research lead" in rheumatoid arthritis has been the invariable remissions or periods of temporary relief that accompany pregnancy and jaundice. Dr. Hench believed that these remissions are not actually from unrelated causes but from the same conditions in the human body. Some biologic change that takes place in the body of a pregnant woman is apparently the same as a change that occurs in jaundice. If this is so, Dr. Hench reasoned, the body may produce an "antirheumatic substance X" that is more plentiful in pregnancy and in jaundice. After much experimentation, Dr. Hench conjectured that substance X might come from the suprarenals. These glands get their name (pronounced *supra-reenal*) from their location just above the kidneys.

What factors furnished the clue in this conjecture? For one, the suprarenal glands of an unborn child are oversized and enormous quantities of hormones are passed into the body of the mother. For another, bilirubin, or red bile, which is poured into the blood stream in large amounts when jaundice occurs, contains many of the chemicals found in suprarenal hormones. Further, experiences that stimulate the suprarenal glands, such as anesthesia or surgery, frequently result in short remissions of rheumatoid arthritis.

For these reasons, Dr. Hench was greatly interested in Dr. Kendall's discovery of Compound E from the very first. When Merck and Company made a quantity of cortisone available to him in 1948, he expressed the belief that its value in rheumatoid arthritis could be tested in a short time.

Compound E Is Substance X

Dr. Hench's belief proved correct. The first patient on whom cortisone was tried was a married woman, 29 years old, who had been afflicted with rheumatoid arthritis for four and a half years. Her joints were swollen, stiff and painful. The typical joint destruction had already begun in her right hip.

On September 20, 1948, she received an injection into her muscles of a small amount—100 milligrams—of cortisone. The injections were repeated on September 21 and 22, although significant improvement in the patient's condition was not noted. On September 23 the soreness in her joints diminished. On September 24 the patient, who had been unable to walk three days previously, walked with only a slight limp.

Injections of 100 milligrams a day were kept up for eight days. At the end of the week the patient, who had formerly been confined to her bed, was able to go on a three-hour shopping expedition in downtown Rochester. The stiffness in her joints had almost completely disappeared. Tenderness and swelling remained to a certain degree, but they may well have been the results of her chronic illness.

In the first test, cortisone was used on fourteen patients with rheumatoid arthritis, all of them severe cases, with excellent results in all. Crutches and wheelchairs were discarded, stiff joints became supple, bent knees straightened out, swelling and pain decreased, appetite and weight increased and the depression that often goes with this disease gave way to well-being.

What Does This Mean to You?

At this writing, nothing except hope.

Your hope for relief may materialize in a few short months. But several years may be required before the many problems involved in treating you with cortisone are solved.

Dr. Hench prefers not to have the results of his work referred to as a treatment at present, for important research remains to be done. The effects of overdosage, to cite an example, must be tested thoroughly.

A Question of Supply

Supply is the greatest problem. Present methods of production were evolved by Dr. Kendall and by Dr. L. H. Sarett of Merck and Company laboratories. They require a basic ingredient known as desoxycholic acid, which is obtained from the bile of oxen. Only one pound of this ingredient can be obtained from one hundred and thirty pounds of bile. A hormone called ACTH, similar in effect to cortisone, can be obtained only in a tiny gland, the pituitary, from hogs. It takes twelve hundred hogs to yield a single pound of the gland substance—in which ACTH is only a small fraction. Science must discover some natural source more

plentiful than these, or achieve a synthetic method—a way to make cortisone or ACTH from raw chemicals—before your family doctor will be able to treat you with the hormones.

Not a Cure

According to Dr. Hench's results, cortisone cannot be given for a few days or weeks and *cure* arthritis. The effect lasts only while the hormone is taken daily, in doses of 75–100 milligrams. A sharp relapse occurs a few days after the injections cease.

So far, cortisone has been found effective only in rheumatoid arthritis. It may prove valuable in the treatment of other rheumatic diseases such as rheumatic fever, Marie-Strumpell disease, gout and fibresitis. Indeed, cortisone *may* be useful in cases of Addison's disease, mental illness, asthma, migraine and other ailments.

Research Made It Possible

Cortisone, like insulin, penicillin and countless other specifics used in man's fight against disease, is a triumph of medical research. But cortisone, which today costs almost a hundred dollars for a single injection, is at best a highly effective palliative—a means of relief while it is being taken. A cure for rheumatoid arthritis and for other rheumatic diseases is yet to be found. It can be found only through additional research.

Medical research works for you—give it your support. Medical research is expensive—it needs your support.

The Arthritis and Rheumatism Foundation recently made a survey of seventy schools of medicine in the United States. The survey disclosed that two hundred and twenty-two research projects in rheumatic disease were being conducted at fifty-one of these institutions. All seventy institutions expressed strong interest in doing more research if financial support could be obtained.

The People Say...

The following comments are representative of the views expressed by the ROUND TABLE *audience on "How To Live a Hundred Years Happily!" broadcast on November 6, 1949. Dr. John A. Schindler of the Monroe Clinic, Monroe, Wisconsin, and Robert J. Havighurst, professor of education at the University of Chicago, were participants. The* ROUND TABLE *wishes to thank the thousands of listeners who have written for copies of this discussion.**

*

Enjoyable and Instructive

The ROUND TABLE program in which Dr. Schindler took part was one of your most enjoyable and instructive programs.—*A listener from Jacksonville, Florida.*

Sixtieth Birthday

On my sixtieth birthday, November 6, I turned the radio dial to your program and heard the most opportune, stimulating, inspiring discussion on old age....

You do not realize how much good you did on that Sunday. I was feeling too sorry for myself—children married and gone, and arteries hardening even if my heart is young and gay! I'm all mixed up inside now that I don't feel essential....

Please send me your pamphlet on old age—I don't feel old, but bosses think you are. I'll carry it in my purse.—*A listener from Hollywood, California.*

Best on Air

I should like to congratulate the doctor who led that discussion. It was to me the best medical discussion in view of good presentation and applicability which I have ever heard presented on the air.—*A listener from Phoenix, Arizona.*

Many Suggestions

Thanks so very much for "How To Live a Hundred Years Happily!" I just made up my mind last night to do my best for the old men and women in our old folks hospital here. I got many fine suggestions from the broadcast.—*A listener from Seattle, Washington.*

Good Reading

I hope I am not too late to obtain three copies of the broadcast "How To Live a Hundred Years Happily!" I want to share it with a couple of friends. That particular discussion was one of the best. What good reading that would be in our daily papers, instead of the usual sensational headlines. It is the University of Chicago ROUND TABLE—and all too few others like it—that makes radio worth while.—*A listener from Chicago, Illinois.*

* Copies of ROUND TABLE Pamphlet No. 607, which contains the text of the discussion on "How To Live a Hundred Years Happily!" and a special article by Mr. Havighurst entitled "Old Age—an American Problem" can still be obtained for 10 cents each from The University of Chicago ROUND TABLE, Chicago 37, Illinois.

Splendid

It was indeed a splendid program. The work you are doing is *outstanding.—A listener from Los Angeles, California.*

Uplifting

I think "How To Live a Hundred Years Happily!" was the most informative and uplifting message that I have heard in a long time.—*A listener from Los Angeles, California.*

To Grandchildren

I am a man of eighty-one years. Had I the information given in this broadcast years ago, I would have benefited by same, therefore I would like to have a copy so that I might pass this information on to my grandchildren and in-laws.—*A listener from Portsmouth, Virginia.*

Again?

We *very* much enjoyed Dr. Schindler of Monroe, Wisconsin, and hope to hear him again soon over your interesting program.—*A listener from Portland, Oregon.*

Thank You

I heard yesterday's talk on the air and wish to thank you for presenting such splendid things to the public.—*A listener from Terrell, Texas.*

Better Outlook

I plan on carrying a copy at all times in my purse and am looking forward to a better outlook on life and health.—*A listener from Iowa City, Iowa.*

Clear and Logical

So many of my friends have joined me in admiration of your broadcast featuring Dr. Schindler and his advice to aging people. It was clear, logical, and very helpful, and I hope to hear other broadcasts on similar themes.—*A listener from Cleveland, Ohio.*

"Humdinger"

Your program tonight must have been a humdinger. Both participants should reach a hundred for that pep talk.—*A listener from Maplewood, New Jersey.*

Wants Others

Your program on "How To Live a Hundred Years Happily!" was the most interesting you have presented in a long time. I hope you will arrange others along this line.—*A listener from Oxnard, California.*

Daily

I enjoyed the program so much, and I should like to have it in print so that I could read it and digest his wonderful advice at my leisure—and daily.—*A listener from Boonton, New Jersey.*

The Best Medicine

I found that the information given by Dr. Schindler is surely the very best medicine for a sick person. I am thankful that I heard him. As for myself, I need just such instruction. I was somewhat at a loss myself to find happiness, but I picked right up after this lecture! Thank you kindly.—*A listener from New York, New York.*

Only Forty Left

Will you please send the recipe for living one hundred years happily, as I have only forty of them left.—*A listener from Los Angeles, California.*

Very Well Told

I enjoyed every minute of last Sunday's broadcast. It was very well told, with nice speakers. Many thanks for a nice half-hour.—*A listener from Woodhaven, New York.*

Can Help Selves

In my opinion this program covered the most important steps or rules for anyone to follow to maintain a balanced and happy viewpoint. In my personal experience, a nerve case developed into all kinds of aches and pains. I have tried the usual helps, and I have come to the conclusion that patients can help themselves. It is only a question of selling them on a balanced and healthy activity which will overshadow and gradually shove the trouble into a secondary or trivial part of their thinking.—*A listener from Dallas, Texas.*

"Hit the Nail on the Head"

You certainly know what you are talking about, Dr. Schindler. We enjoyed and learned very much, listening to your very interesting discussion. You surely hit the nail on the head, in my case, and also my mother's—very decidedly.—*A listener from Seattle, Washington.*

True Meaning of Happiness

I have wondered about the definition or true meaning of happiness, which is of the moment, and more or less of the spontaneity of children. Is it not the joy of living and joy in life and its more wholesome quality that we should achieve as we grow older? Happiness is of the moment. But joy abides and is spiritual.—*A listener from Indianapolis, Indiana.*

We All Need It

I do enjoy your ROUND TABLES—especially the one today on "How To Live a Hundred Years Happily!" We all need Dr. Schindler's prescription.—*A listener from Portland, Oregon.*

Really Stimulating

It was really very stimulating and so true. The more we follow Dr. Schindler's advice, the better off we will be. Thanks for an excellent and educational program.—*A listener from St. Louis, Missouri.*

Living Conditions

Both Dr. Schindler and Mr. Havighurst were very good. There was so much truth in both of their statements. The trouble with most people when they get past fifty is that they fall into a rut. I am almost 56 myself and have rheumatic heart trouble, but I try to be as cheerful as I can, and see the humor in everyday life. But sometimes I get down.

I thought what you said about old people having better living conditions was especially good. I think we need them in every city in America.—*A listener from Beloit, Wisconsin.*

Wonderful

It was a perfectly wonderful and enlightening broadcast.—*A listener from Providence, Rhode Island.*

Agrees with Bible

The discussion on happiness in old age was most interesting. I have a similar idea of longevity. It also harmonizes with the Bible—see Psalms 34:11-13, also II Corinthians 7:10.—*A listener from LaCrosse, Wisconsin.*

Did You Hear These ROUND TABLE *Discussions—*

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